

REMARKS

Reconsideration of the Office Action mailed March 3, 2004, (hereinafter "instant Office Action"), entry of the foregoing amendments, withdrawal of the objection to claims 37 and 38 and withdrawal of the rejection of claims 16-26 and 36, and are respectfully requested.

In the instant Office Action, claims 16-26 and 36-38 are listed as pending, claims 37 and 38 are listed as objected to and claims 16-26 and 36 are listed as rejected.

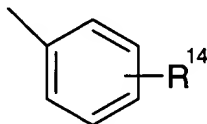
Claim 16 has been amended at lines 14-21 to clarify the claim with respect to "substituted and unsubstituted" and "suitable substituents". Support for these amendments can be found at page 17, lines 6-9, *inter alia*, of the instant application. No new matter has been added.

The Examiner does not reiterate in the instant office action: the rejection of claims 16 and 36 under 35 U.S.C. §102(b), as allegedly being anticipated by Gasprova *et al.*, Chem Abstract 124: 55745; the rejection of claims 16 and 36 under 35 U.S.C. §102(b), as allegedly being anticipated by Kawashima *et al.* (WO 95/13269); the rejection of claims 16 and 36 under 35 U.S.C. §102(b), as allegedly being anticipated by Hamari *et al.*, Chem Abstract 103:142032; the rejection of claim 16 under 35 U.S.C. §102(b), as allegedly being anticipated by McCarthy *et al.*, Chem. Abstract 110:38945; the rejection of claims 16 and 36 under 35 U.S.C. §102(b), as allegedly being anticipated by Maki *et al.* (U.S. Patent 4,490,292); the rejection of claims 16 and 36 under 35 U.S.C. §102(b), as allegedly being anticipated by Anzai *et al.*, Chem Abstract 82:140162; or the rejection of claims 16 and 36 under 35 U.S.C. §102(b), as allegedly being anticipated by Sakuta *et al.*, Chem Abstract 119: 63033. Applicants assume that these rejections do not appear in the instant office action because the arguments and amendments submitted in the Preliminary Amendment that accompanied the Request for Continued Examination filed January 22, 2004 overcame the aforementioned rejections and that said rejections are withdrawn.

The Examiner has rejected claims 16 and 36 under 35 U.S.C. §102(b), as allegedly being anticipated by Varano *et al.*, Chem Abstract 131: 44782. The Examiner alleges that the instantly claimed compounds read on the reference compound, specifically RN 227012-80-8 and RN 227012-82-0. Applicants have amended claim 16 to proviso out RN 227012-80-8 and RN 227012-82-0. Thus the rejection of claims 16 and 36 under 35 U.S.C. §102(b), as allegedly being anticipated by Varano *et al.*, is obviated and should be withdrawn.

The Examiner has rejected claims 16, 17 and 36 under 35 U.S.C. §102(b), as allegedly being anticipated by Krapcho *et al.*, (J. Med. Chem., 1973). The Examiner alleges that the instantly claimed compounds read on the reference compound, see Table III, page 779, especially compounds b, d, f. Applicants respectfully point out that in the Preliminary Amendment that accompanied the Request for Continued Examination filed January 22, 2004 Claim 16 was amended to proviso out compounds b, d, and f as well as compound g of Table III of Krapcho *et al.* Applicants respectfully remind the Examiner that compounds a, c, e and h in Table III are specifically excluded by the original proviso in Applicants' claim 16 which states:

when X is O and n is 0, R¹ is hydrogen or a substituted or unsubstituted aliphatic group and R is a substituted or unsubstituted aromatic or aralkyl group, ***provided that R is not*** thiophenyl, benzoxadiazolyl, 3-furanyl, **3-pyridinyl** or



where R¹⁴ is H, CF₃, phenyl, OCH₃, -O-phenyl, NO₂ or -OC(O)CH₃...

Therefore, Krapcho *et al.*, does not anticipate Applicants' amended claim 16.

Based upon the foregoing, the rejection of claims 16, 17 and 36 under 35 U.S.C. §102(b) over Krapcho *et al.* is obviated and should be withdrawn.

The Examiner has rejected claim 16 under 35 U.S.C. §102(b), as allegedly being anticipated by Shah *et al.*, Chem Abstract 78: 124527. The Examiner cites the compounds having RN 415265-86-7, 41526-87-8, 41526-88-9, 41526-89-0, -90-3, -91-4, -92-5, -93-6, 94-7, and -95-8. Claim 16 has been amended to exclude these compounds. Thus, the rejection of claim 16 under 35 U.S.C. §102(b), as allegedly being anticipated by Shah *et al.*, is obviated and should be withdrawn.

The Examiner has rejected claims 16 and 36 under 35 U.S.C. §102(b), as allegedly being anticipated by Gezginici *et al.* (Farmaco, 1997). The Examiner alleges that Gezginici *et al.* teaches the compounds and compositions of the instant invention (see Table 1). Applicants respectfully traverse this rejection. Compounds IIIa-IIIh in Table I do not anticipate claims 16 and 36 because each of these compounds has an oxygen in the "Y" position adjacent to the

methylene on the heterocyclic ring. In the instant invention, "Y" can only be -S-, -SO- or -SO₂-. Gezginci *et al.* does not teach or suggest -S-, -SO- or -SO₂- in this position. Therefore, the rejection of claims 16 and 36 under 35 U.S.C. §102(b), as allegedly being anticipated by Gezginci *et al.* (Farmaco, 1997) is obviated and should be withdrawn.

The Examiner has rejected claims 6 and 36 under 35 U.S.C. §103(a) as allegedly being unpatentable over Krapcho (US 4,078,062). The Examiner alleges that the reference teaches a generic group of compounds which embraces Applicants' instantly claimed compounds. Applicants presume that the Examiner means claims 16 and 36, as claim 6 is cancelled. Applicants respectfully traverse this rejection. The Examiner has not established a *prima facie* case of obviousness. In order for an invention to be considered obvious under 35 U.S.C. 103(a), the invention must be considered as a whole, there must be some motivation or suggestion in the prior art reference itself to modify the reference, and there must be a reasonable expectation of success.

The Court of Appeals for the Federal Circuit has stated the following on the issue of obviousness:

Uniroyal, Inc. v. Rudkin-Wiley Corp., 837 F. 2d 1044, 1051-52, 5 USPQ 1434, 1438 (Fed. Cir. 1988), cert. denied, 109 S. Ct. 75 (1988), on remand, 13 USPQ2d 1192 (D. Conn. 1989) "Something in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination."; In re Stencel, 828 F. 2d 751,755, 4 USPQ2d 1071, 1073 (Fed. Cir. 1987) obviousness cannot be established "by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion that the combination be made." Alco Standard Corp. v. Tennessee Valley Authority, 808 F. 2d 1490, 1498, 1 USPQ2d 1337, 1343 (Fed. Cir. 1986), cert. dismissed, 108 S. Ct. 26 (1987) "the question is not simply whether the prior art 'teaches' the particular element of the invention, but whether it would 'suggest the desirability, and thus the obviousness, of making the combination.'"; Carella v. Starlight Archery, 804 F. 2d 135,231 USPQ 644 (Fed. Cir. 1986); ACS Hospital Sys., Inc. v. Montefiore Hospital, 732 F. 2d 1572, 221 USPQ 929 (Fed. Cir. 1984) "Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under section 103, teachings of references can be combined only if there is some suggestion or incentive to do so."

Donald S. Chisum, Patents, A Treatise on the Law of Patentability, Validity and Infringement, Vol. 2, 5-218, 1992.

In Formula I of Krapcho (US 4,078,062), the phenyl is directly attached to the methylene. In the instant application, the aromatic group may be connected to the methylene via an optionally substituted amino linker. Krapcho does not teach or suggest an amino linker. Further, in Krapcho's Formula I the phenyl is linked to another group, B, by way of an -O- or -O-alkyl linker. One of these linkers is always present. In the instant application an -O- or -O-alkyl linker in this position is not a required part of the basic molecule. In another difference, the core of Krapcho is limited to a benzothiazine, whereas in the instant application the core can also be benzothiazine oxide or benzothiazine dioxide. Additionally, "X" in the instant application can be S, O or NOR³. In Krapcho this position is limited to oxygen. Krapcho does not teach or suggest any of these differences.

The Examiner states that "[i]t has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus and cites In re Susi, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in Merck & Co. v. Biocraft Laboratories, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989). In In re Susi, the Appellant's composition of matter claims was rejected under 35 U.S.C. §103(a) over the combination of three references, Knapp, Lauerer and Costello. With respect to Knapp, there was only one important difference between it and the Appellant's application. Knapp showed a hydroxyl group attached to the benzene ring which was absent in the Appellant's formula. In contrast, claim 16 of the instant application differs in several respects from Krapcho, as discussed above.

Lauerer disclosed a large genus which Appellants pointed out undeniably included at least some of the compounds recited in Appellant's generic claims and it was a class of chemicals to be used for the same purpose as Appellant's additives. In the instant case, Krapcho discloses a smaller genus than that described in the instant application,

Costello taught protection of polystyrene from ultraviolet light-induced deterioration by the addition of a trialkyl phenol and discloses as the best of the specific examples given, a particular phenol which was recited in Appellant's claims 12 and 13. By contrast, Krapcho does not disclose any of the species claimed or exemplified in the instant application. Thus, In re Susi is not on point.

The Examiner also cites Merck & Co. v. Biocraft Laboratories, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989). In Merck & Co., the issue was whether the US 3,781,430 patent (the '430 patent) was invalid for obviousness over Merck's own US 3,313,813 patent (the '813 patent). The '430 patent claimed the 1:10/5 mg:50 mg amiloride/hydrochlorothiazide combination as a diuretic formulation. The '813 patent disclosed that various guanidines, including amiloride, were effective diuretic agents and identified hydrochlorothiazide as an example of a potassium excreting diuretic with which the claimed compounds can be combined. The question was whether the '813 patent taught the 1:10/5 mg:50 mg amiloride/hydrochlorothiazide combination as a diuretic formulation. Merck failed to show unexpected results with the claimed combination and in addition, the court found that the claimed dosage was arrived at using routine procedures and producing only predictable results. As such, the recited dosages therefore did not distinguish the claims of the '430 patent from the amiloride/hydrochlorothiazide combination disclosed in the '813 patent.

Merck & Co is not on point because it concerns a claim directed to a particular ratio of ingredients in a pharmaceutical composition. A case that is more relevant to the instant rejection is In re Jones, 958 F.2d 347 (1992). In In re Jones, the Examiner rejected a claim to the 2-(2'-aminoethoxy)ethanol salt of dicamba as obvious over U.S. Patent No. 3,013,054 ("Richter") and 86 Chem. Abstracts No. 437711a ("Wideman"). Richter disclosed a genus which admittedly encompassed the claimed salt but did not specifically disclose the claimed 2-(2'-aminoethoxy)ethanol salt. Richter did not teach the amine needed to prepare this salt, but Wideman did. Wideman, however, was directed to the use of that amine in the preparation of surfactants for shampoos, bath preparations, and emulsifiers. The Board of Appeals upheld the Examiner's obviousness rejection and also noted structural similarity between the claimed salt and the disclosed genus in the prior art. The CCPA, however, found that a disclosure of a chemical genus does not render obvious a species that happens to fall within it. The CCPA also found that there was not close structural similarity because the claimed salt was a primary amine with an ether linkage, whereas the diethanolamino salt disclosed by Richter is a secondary amine without an ether linkage. Thus, the CCPA concluded that the Examiner had failed to establish a *prima facie* case of obviousness.

Although In re Jones deals with the species-genus relationship with respect to obviousness, it is applicable to the instant case. In In re Jones a genus was disclosed which encompassed the Appellants' claimed compound. In the instant case the reference, Krapcho describes a genus which overlaps with Applicants' claimed genus. However, as with Richter in Merck & Co., Krapcho does not disclose any of the species claimed or exemplified in the instant application. Krapcho's genus does not make Applicants' genus as a whole obvious. An invention is to be considered as a whole. The claimed invention may not be dissected into discrete elements to be analyzed in isolation, but must be considered as a whole. See, e.g. W.L. Gore & Assoc. Inc. v. Garlock, Inc. 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983)); Jones v. Hardy, 727 f.2d 1524, 1530, 220 USPQ 1021, 1026 (Fed. Cir. 1983). In determining the differences between the prior art and the claims, the question under 35 U.S.C. §103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); Schenck v. Nortron Corp., 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983). The Examiner has not shown how Krapcho renders obvious the entire genus of Applicants' claim. Applicants maintain that Krapcho does not render claims 16 and 36 obvious.

Based upon the foregoing, the rejection of claims 16 and 36 under 35 U.S.C. §103(a) over Krapcho (US 4,078,062) is obviated and should be withdrawn.

The Examiner has rejected claims 16-26 under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons:

- 1) Claim 20 recites the limitation of a formula starting from the third line. There is insufficient antecedent basis for this limitation in the claim. The formula the Examiner refers to is a species to be excluded from claim 16 which appears in claim 20 due to an inadvertent formatting error. Applicants have deleted the formula from claim 20 and inserted it at the end of the proviso in claim 16.
- 2) The phrases "substituted with suitable substituents" and "substituted or unsubstituted" throughout claims 16-26 and 36 are unclear as to the nature and number of substituents. Applicants respectfully direct the Examiner's attention to page 11, line 23 to page 12, line 22 wherein a definition of "suitable substituents" is provided.

Based upon the foregoing, Applicants believe that claims 16-26 and 36 are in condition for allowance. Prompt and favorable action is earnestly solicited.

No fees are due for the instant amendment since the total number of claims after entry of the amendments hereinabove is not more than the total number of claims that Applicants have paid for to date.

If the Examiner believes that a telephone conference would advance the condition of the instant application for allowance, Applicants invite the Examiner to call Applicants' agent at the number noted below.

Respectfully submitted,

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